US ERA ARCHIVE DOCUMENT

MEMORANDUM:

SUBJECT: Imazalil, Reregistration. Nature of the Residue in Ruminant (MRID Nos. 42454801, 42454802, and 42593602), and Analytical Methods for Plants (MRID Nos. 42454803 and 04). CBRS Nos. 10589 and 11220. DP Barcode Nos. D182706 and D186541.

FROM:

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THRU:

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Registrant Janssen Pharmaceutica, in support of reregistration, has submitted a metabolism study of imazalil in goat, and data on analytical methods in banana and citrus fruit. Assignment instructions are to review the submitted data for reregistration. Tolerances are established for combined residues of the fungicide imazalil, 1-[2-(2,4-dichlorophenyl)-2-(2-propenyloxy)ethyl]-1H-imidazole and its metabolite 1-(2,4-dichlorophenyl)-2-(1H-imidazole-1-yl)-1-ethanol, in or on crop commodities (40 CFR 180.413(a)), and for combined residues of imazalil and its metabolites 1-(2,4-dichlorophenyl)-2-(1H-imidazole-1-yl)-1-ethanol and 3-[1-(2,4-dichlorophenyl)-2-(1H-imidazole-1-yl)ethoxyl]-1,2-propane diol in or on animal commodities (40 CFR 180.413(b)). Imazalil is a List B Chemical. Phase 4 Review of Residue Chemistry data requirements was issued

Conclusions

10/19/90 (S.R. Funk).

- 1. In liver, the HCl hydrolysis fraction (10.2% TRR, 2.18 ppm) and unextractables (12.5% TRR, 2.68 ppm) represented greater than 10% total radioactive residue (TRR) and greater than 0.05 ppm, but were not further analyzed. Unextracted and unanalyzed residues in tissues other than liver represented less than 10% of TRR or less than 0.05 ppm.
- 2. Parent imazalil was identified as 6.6% of TRR in fat, and smaller portions in other tissues. Major metabolites identified or characterized were FK1524, 29.7% of TRR in

122

CBRS 10589, Imazalil, Metabolism in Goat, p. 2 of 16

fat; FK284, 14.4% of TRR in muscle and 11.0% of TRR in fat; FK772, 15.1% of TRR in kidney and 20.2% of TRR in muscle; and MS4, 10.9% of TRR in milk (see Figures 2 and 4 for structures).

- 3. The portion of the total radioactive residue characterized and/or identified ranged from 26.3% in liver to 53.9% in fat. Unidentified metabolites each represented less than 10% TRR or less than 0.05 ppm, in all tissues except liver.
- 4. Registrant should provide frozen storage data for the samples analyzed in Supplement 1 to Report R23979/FK1206 (identification of aqueous phases from milk, liver, and kidney). If samples were stored for more than 6 months, registrant should provide storage stability data. Ideally, data should indicate that the identity of residues did not change during the period between collection and final analysis. If data are not available to indicate chromatographic profiles of extracted samples shortly after collection, then data indicating that total radioactivity in the fractions of interest did not change significantly during storage would be acceptable.
- 5. This assignment also included documents on analytical methods in plants (MRID 42454803 and 04). The assignment under DP Barcode No. D182707, CBRS No. 10602 consists of another analytical method in plants (MRID 42454805). For more efficient review, the analytical methods under this assignment will be transferred to CBRS No. 10602 and will be reviewed as part of that assignment.

Note to PM: MRIDs 42454803 and 04 will be transferred to DP Barcode No. D182707, CBRS No. 10602, and will be reviewed under that assignment.

Recommendations

The characterization and/or identification of residues analyzed is satisfactory, but further work is necessary to upgrade this metabolism study to an acceptable level. Data should be submitted to resolve Conclusions 1 and 4 above. The residues in liver remaining after initial methanol and methanol:water extraction should be extracted by exhaustive methanol Soxhlet treatment. If residues greater than 10% of liver TRR are released by this treatment, they should be further extracted, if appropriate, and analyzed. The identity of any metabolite representing greater than 10% of TRR and greater than 0.05 ppm should be confirmed by a second method. Such analysis should be supported by appropriate storage stability data. If data are not available to indicate chromatographic profiles of extracted samples shortly after collection, then data indicating that total radioactivity in the fractions of interest did not change significantly during storage would be acceptable.

CBRS 10589, Imazalil, Metabolism in Goat, p. 3 of 16

Reregistration Requirements

Phase 4 Review of imazalil identified the following requirement for nature of the residue in animals (10/19/90, S.R. Funk):

The registrant must provide a goat/cow metabolism study and a poultry metabolism study. Imazalil labeled in a non-labile part of the molecule should be fed to the livestock for a minimum of three days. Orally treated test animal must be sacrificed within 24 hours of the final dose. The dose administered and the specific activity should be high enough to allow for adequate identification of the metabolites/degradates. The tissues from the metabolism study should be tested using the data collection method(s) and enforcement analytical method(s).

A protocol for a metabolism study in goat has been reviewed (CBRS No. 7997, 7/2/91, S.R. Funk). The protocol was acceptable with three changes: (1) A confirmatory method in addition to TLC was required for the identification of metabolites; (2) Impurities in the test substance should be determined via methods used to analyze metabolites and via methods routinely used for the analysis of impurities in technical imazalil; (3) Sources of the reference compounds and limited structural/purity information must be provided.

Metabolism Protocol

Registrant's present submissions on goat metabolism are:

¹⁴C-Imazalil: Distribution, Degradation, Metabolism and Excretion After Repeated Oral Administration to a Lactating Goat, Janssen Report No. R23979/FK1206, July 22, 1992 (MRID 42454801), and

Supplement to Janssen Report No. R23979/FK1206, August 14, 1992 (MRID 42454802) [referenced below as Supplement 1], and

Supplement 2 to Janssen Report No. R23979/FK1206, October 19, 1992 (MRID 42593602).

The performing organization for animal dosing and laboratory analysis was RCC Umweltchemie, Itingen, Switzerland. Structures of imazalil and related compounds are indicated in Figure 2. It should be noted in Figure 2 that compound FK411 is the ethanol metabolite included in the tolerance expression for plant and animal commodities, and compound FK858 is the propane diol metabolite included in the tolerance expression for animal commodities. The test substance was the sulfate salt of [14C]imazalil, labeled in the carbon directly attached to the phenyl ring. Radiochemical purity was approximately 98%; TLC analysis of the label indicated one

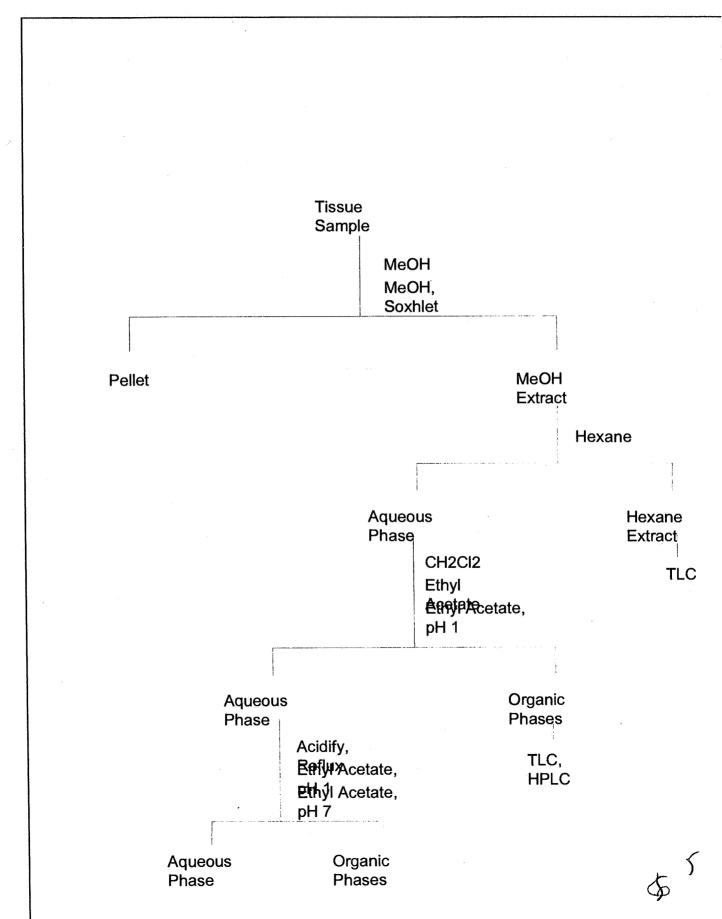
strong peak representing parent and two minor contaminants, one of which migrated near the origin. Label was mixed with unlabeled imazalil to a specific activity of 4.5 μ Ci/mg. A lactating goat was fed twice daily by intubation at a daily dose of 10.4 ppm in the diet. Doses were administered approximately 30 min after morning and afternoon milking; milking was also performed just prior to sacrifice. Blood samples were taken immediately prior to each administered dose. The animal was sacrificed 16 h after the final dose. Liver, kidney, muscle, and fat were removed. Weights of whole tissues were recorded, organs and tissues were homogenized, and homogenates were stored at -20°C until additional analyses.

Total radioactive residues (TRR) in tissue samples were detected by homogenizing tissues, combusting, and counting by liquid scintillation. Residues are summarized in Table 1; milk residues reached a plateau at 0.991 ppm after the sixth dose. Background levels for an untreated goat were no more than 0.021 ppm for any tissue:

Table 1. Total Radioactive Residues in Goat Tissues.

Tissue	Total Radioactive Residue, ppm:
Liver	19.8
Kidney	9.6
Muscle	0.362
Fat	0.091
Milk	0.991

The extraction protocol was similar for kidney and muscle, and is outlined in Figure 1. Extraction protocols for liver, milk, and fat included some common steps, but were not identical to the scheme in Figure 1. Samples of 20 g kidney or 210 g muscle were extracted three times with methanol and once with methanol:water (8:2). Tissue pellets were then extracted for 16 h with methanol in a Soxhlet apparatus. Methanol extracts were combined and concentrated under reduced pressure. The remaining aqueous phase was diluted with acetonitrile (1:1) and partitioned twice, each with an equal volume of hexane; the combined hexane phases were analyzed by TLC. Acetonitrile was evaporated under reduced pressure, and the remaining aqueous phase was partitioned twice with dichloromethane and ethyl acetate under neutral conditions (1:2, v:v). The aqueous phase was acidified with HCl to pH 1.0, and partitioned once or twice with ethyl acetate. The resulting organic phases dichloromethane, ethyl acetate, and acidified ethyl acetate, were combined and analyzed by TLC and HPLC. The resulting aqueous phase was acidified with 4N HCl (1:3), hydrolyzed for 16 h at 70°C by refluxing, and partitioned with ethyl acetate under acidic and neutral conditions.



Liver aliquots of 20 g were extracted twice with methanol and methanol:water. The pellet was additionally extracted with acetonitrile and methanol:ammonia, pH 10. The resulting pellet was hydrolyzed in 0.01 M HCl for 16 h at 70°C. This acid extraction resulted in a turbid suspension of high viscosity. The methanol fractions were extracted as in Figure 1, except for an additional extraction of the aqueous phase after hexane extraction, with ethyl acetate at pH 10. This protocol resulted in an overall extraction of 80% TRR. Additional procedures were attempted, including the methanol Soxhlet procedure described for kidney and muscle. However, none of these procedures improved recovery of radioactivity, so the extracts from the initial procedure with liver were used for analysis.

An aliquot of 20 ml milk, taken after the last administered dose, was centrifuged for 15 min at 1900 g. After removal of fat, defatted milk was deproteinated by addition of acetone (1:4, v:v). The mixture was incubated for 16 h at 4°C, and centrifuged for 15 min at 1900 g. The supernatant (whey) was removed and the remaining protein pellet was washed with 40 ml acetone and then extracted with about 40 ml methanol. The whey, acetone wash, and methanol extract were combined, and treatment of this mixture was similar to the protocol in Figure 1, starting with hexane partitioning. The aqueous phase from hexane extraction was extracted successively with dichloromethane, ethyl acetate, dichloromethane at pH 1, and ethyl acetate at pH 1. The aqueous phase after acidification and refluxing was partitioned with ethyl acetate under acidic, neutral, and basic conditions. The resulting organic phases were combined, evaporated nearly to dryness, redissolved in acetone, and analyzed by TLC.

An aliquot of 100 g fat was extracted three times with dichloromethane, followed by acetonitrile and acetonitrile: chloroform (1:2). The remaining pellet was extracted with methanol followed by extraction with methanol in a Soxhlet apparatus. The organic extracts were combined and evaporated to dryness. The fat residue was redissolved in hexane and partitioned with acetonitrile. The acetonitrile phase was concentrated, mixed with dichloromethane, and analyzed by TLC.

Tables 2 through 5 summarize distributions of radioactive residues for each of kidney, muscle, liver, milk, and fat. Of the fractions in Table 2 from kidney, hexane (5.0% TRR) and combined dichloromethane/ethyl acetate extracts (43.1% TRR) were separately analyzed. In registrant's initial report, other



CBRS 10589, Imazalil, Metabolism in Goat, p. 7 of 16

fractions from kidney were not analyzed, including the aqueous phase (32.8% TRR). In muscle, the hexane (5.9% TRR) and the combined dichloromethane/ethyl acetate extracts (65.3% TRR) were separately analyzed; other fractions were not further analyzed.

Table 2. Distribution of Radioactive Residues, Kidney and Muscle.

	Residue in Kidney, Residue in Muscle % TRR (ppm) % TRR (ppm)	
Extract		
MeOH Soxhlet	6.5 (0.628)	4.7 (0.016)
Organic extracts:		
Hexane	5.0 (0.483)	5.9 (0.020)
Dichloromethane	23.3 (2.251)	47.8 (0.165)
Ethyl acetate	8.3 (0.802)	15.9 (0.055)
Ethyl acetate, pH 1	11.5 (1.111)	1.6 (0.005)
Aqueous phases after acid hydrolysis:		
Ethyl acetate	4.0 (0.386)	6.1 (0.021)
Ethyl acetate, pH 7	5.2 (0.502)	5.2 (0.018)
Aqueous phase	32.8 (3.169)	10.6 (0.037)
Totals	96.6 (8.704)	97.8 (0.321)

Table 3 summarizes the distribution of residues in fractions from liver, for the protocol where samples were taken for further analysis. Of the organic fractions, hexane (6.0% TRR) and dichloromethane/ethyl acetate extracts (31.9% TRR) were separately analyzed. The final aqueous phase (20.6% TRR) was also analyzed. Registrant reported that the fraction from initial HCl hydrolysis was turbid and highly viscous, and was not further analyzed, nor were other fractions:

CBRS 10589, Imazalil, Metabolism in Goat, p. 8 of 16

Table 3. Distribution of Radioactive Residues in Liver.

Extract	Residues, % TRR	Residues, ppm
Initial HCI hydrolysis	10.2	2.18
Organic extracts:		
Acetonitrile	1.9	0.41
Methanol:ammonia	2.7	0.58
Hexane	6.0	1.28
Dichloromethane	25.5	5.46
Ethyl acetate	6.4	1.37
Ethyl acetate, pH 10	1.1	0.24
Ethyl acetate, pH 2	2.3	0.49
Aqueous phases after acid		
hydrolysis:		
Ethyl acetate	2.2	0.47
Ethyl acetate, pH 7	1.1	0.24
Aqueous phase	20.6	4.41
Unextractable	12.5	2.68
Total	92.5	19.8

Table 4 summarizes the distribution of residues in milk. Of the milk fractions, the combined dichloromethane and ethyl acetate phases, representing 53.8% of TRR were further analyzed. In registrant's initial report, other fractions, including the aqueous phase (23.4% of TRR) after hydrolysis and ethyl acetate extraction, were not further analyzed.

CBRS 10589, Imazalil, Metabolism in Goat, p. 9 of 16

Table 4. Distribution of Radioactive Residues in Milk.

Extract	Residues, % TRR	Residues, ppm
Fat	6.9	0.066
Protein pellet	4.0	0.039
Organic phases:		
Hexane	0.4	0.004
Dichloromethane	13.8	0.132
Ethyl acetate	20.6	0.198
Dichloromethane, pH 1	0.9	0.009
Ethyl acetate, pH 1	18.5	0.177
Aqueous phase after acid hydrolysis:		
Ethyl acetate, acid	6.1	0.059
Ethyl acetate, netural	5.0	0.048
Ethyl acetate, basic	3.6	0.034
Aqueous phase	23.4	0.225
Total	92.3	0.886

Table 5 summarizes the distribution of residues in fat. The acetonitrile extract (61.6% TRR) was further analyzed. Registrant reported that no other fractions were further analyzed because of they all contained low levels of radioactivity.

Table 5. Distribution of Residues in Fat.

Extract	Residues, % TRR	Residues, ppm
Methanol	2.5	0.003
Methanol Soxhlet	1.5	0.001
Hexane	15.3	0.016
Acetonitrile	61.6	0.066
Unextractable	4.8	0.005
Total	85.7	0.09

CBRS Comments, Metabolism Protocol

According to the approved protocol, imazalil was to be labeled in ¹⁴C at the carbon attached to the imidazole ring. Labeling was actually at the carbon attached to the phenyl ring. However, one would not expect significant differences in stability between these two carbons. For the extraction protocol, raw data for counting and representative calculations were provided for fractions in milk.



According to registrant's initial report, the following fractions generated during extraction contained radioactive residues >10% TRR and >0.05 ppm, but were not further analyzed: In kidney, the final aqueous phase (32.8% TRR, 3.17 ppm); in liver, HCl hydrolysis (10.2% TRR, 2.183 ppm) and unextractables (12.5% TRR, 2.68 ppm); in milk, the final aqueous phase (23.4% TRR, 0.225 ppm). It should be noted, however, that the analysis of the aqueous phases of kidney and milk were described in Supplement 1 to registrant's report.

Conclusion 1: In liver, the HCl hydrolysis fraction (10.2% TRR, 2.18 ppm) and unextractables (12.5% TRR, 2.68 ppm) represented greater than 10% TRR and greater than 0.05 ppm, but were not further analyzed. Unextracted and unanalyzed residues in tissues other than liver represented less than 10% of TRR or less than 0.05 ppm.

Identification of Residues

Extracted residues were analyzed by TLC and/or HPLC. TLC was carried out on silica thin layer plates developed in one of multiple systems using organic solvents. Reverse phase HPLC was carried out on a Lichrosorb RP-18 or Lichrosorb RP-8 column, developed in a gradient in ammonium acetate and acetonitrile. Residues were compared in mobility with reference compounds. Reference compounds were dissolved in acetone:methanol, and visualized by iodine vapor and/or ultraviolet light at 254 nm after TLC analysis. All reference compounds indicated one distinct major spot.

Residues characterized by TLC representing greater than 10% of TRR and greater than 0.05 ppm were confirmed in their identity by HPLC, with the exception of unknowns Mi7.4 and MS4, for which further analyses are described below. Metabolites representing smaller proportions of TRR were also often confirmed by HPLC. Other unknowns which could not be correlated with the reference compounds in Figures 2 and 3 represented less than 10% of TRR. Based on the TLC and HPLC analyses, parent and metabolites with the FK designation were assigned in goat tissues as indicated in Table 6 below.

Supplement 1 to Report R23979/FK1206 (MRID 42454802) described additional analyses conducted on fractions from goat tissues. The aqueous phases from milk, liver, and kidney, representing 23.4%, 20.6%, and 32.8% of TRR, respectively, were analyzed by HPLC, using a Waters apparatus, a C-18 column, and elution with a gradient in diethylamine and organic solvents. For aqueous phases from all three tissues, treatment with ß-glucuronidase and/or arylsulfatase had little influence on the HPLC profile, indicating that these enzymes had little effect in releasing conjugated molecules. In liver and kidney, no single HPLC peak represented more than 8% of TRR in the respective tissue, and these unknowns were not further analyzed. An HPLC peak in the aqueous phase from milk, designated MS4, represented about 10.9% of

44

CBRS 10589, Imazalil, Metabolism in Goat, p. 11 of 16

TRR in milk, and was further analyzed by mass spectrometry. HPLC analysis of the milk unknown Mi7.4 revealed 4 peaks. The two strongest peaks, designated MS1 (8.0% of TRR) and MS3 (1.3% TRR), were also further analyzed by mass spectrometry.

Mass spectrometry was carried out on Finnegan MAT 4500 and Finnegan MAT 90 units. Electron impact spectra were obtained. Molecular weight information was obtained from desorption chemical ionization spectra and fast atom bombardment spectra. Compound MS3 displayed a mass spectrum that was identical to that of a reference compound, and its structure was assigned as indicated in Figure 4. Compound MS1 could not be unambigously assigned. Its spectrum was similar, but not identical, to that of FK839, indicating that the imidazole ring was opened. The structure assigned to MS1 is indicated in Figure 4, where R and R' were not determined. The spectra of compound MS4 indicated m/e 345 for the protonated molecular ion. Strong peaks corresponded to the intact 1-methyl-1H-imidazole part of the molecule, and to the 2,4-dichlorobenzoyl fragment. Methylation with diazomethane indicated a carboxylic acid function. On the basis of all spectral data, compound MS4 was assigned the structure indicated in Figure 4.

Table 6 summarizes the overall assignment of imazalil goat metabolites in all tissues. Metabolites FK411, FK274, and FK861 were detected in milk only after acid hydrolysis and subsequent extraction into organic solvents; as Table 6 indicates, these compounds were therefore assumed to be present in milk in conjugated form only. Metabolite assignments were summed over all analyzed fractions for each tissue:

Table 6. Overall Assignment of Imazalil Goat Metabolites.

	% of TRR in: (TRR for each tissue in parentheses)				
Metabolite	Milk (0.99 ppm)	Liver (19.8 ppm)	Kidney (9.6 ppm)	Muscle (0.36 ppm)	Fat (0.09 ppm)
Parent	ND	6.4	3.6	2.5	6.6
FK 1524	ND	ND	ND	ND	29.7
FK 1454	ND	5.0	ND	6.6	ND
FK 274	0.9 (C)	0.6	ND	ND	6.6
FK 411	3.3 (C)	1.0	ND	ND	ND
FK 284	6.2	2.3	ND	14.4	11.0



CBRS 10589, Imazalil, Metabolism in Goat, p. 12 of 16

FK 326	2.2	4.5	2.7	8.0	ND
FK 582	1.3	ND	ND	ND	ND
FK 258	2.9	ND	2.9	ND	ND
FK 858	3.3	2.9	1.5	ND	ND
FK 772	5.3	4.4	15.1	20.2	ND
FK 839	7.0	2.2	0.5	ND	ND
FK 861	0.9 (C)	0.6	ND	ND	ND
MS 1	8.0				
MS 3	1.3				
MS 4	10.9				
Total % TRR Identified	53.5	29.9	26.3	51.7	53.9

Table notes:

ND = nondetectable. (C) = detected only as conjugate.

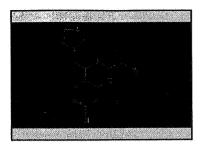
For structures of parent and metabolites, see Figures 2-4.

MS1, MS3, and MS4 were determined only in milk.

For fractions analyzed in Report R23979/FK1206 (MRID 42454801), registrant submitted storage stability data. Registrant noted that the maximum storage period of tissues at -20°C before final analyses were 10 weeks for liver and 17 weeks for milk, kidney, muscle, and fat. Report R23979/FK1206 presented TLC profiles for organic solvent fractions at 0 and 3 months of frozen storage;

Supplement 2 to the Report presented TLC profiles at 0 and 6 months of frozen storage. Profiles were comparable, although not identical, over time. Storage stability data were not provided for aqueous fractions analyzed in Supplement 1 to Report R23979/FK1206 (MRID 42454802).

CBRS 10589, Imazalil, Metabolism in Goat, p. 13 of 16



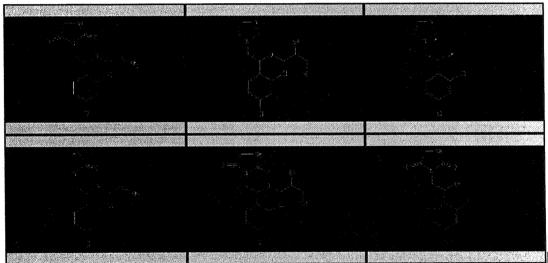


Figure 2.

Imazalil (parent), major goat metabolites, and putative intermediates.

CBRS 10589, Imazalil, Metabolism in Goat, p. 14 of 16

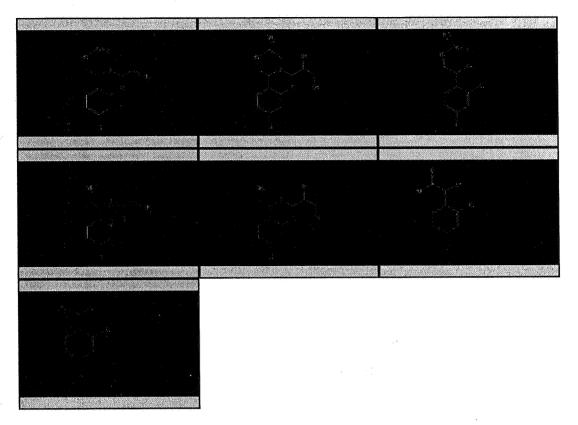


Figure 3. Additional imazalil metabolites in goat.

CBRS 10589, Imazalil, Metabolism in Goat, p. 15 of 16



Additional imazalil metabolites in milk.

CBRS 10589, Imazalil, Metabolism in Goat, p. 16 of 16

CBRS Comments, Identification of Residues

Conclusion 2: Parent imazalil was identified as 6.6% of TRR in fat, and smaller portions in other tissues. Major metabolites identified or characterized were FK1524, 29.7% of TRR in fat; FK284, 14.4% of TRR in muscle and 11.0% of TRR in fat; FK772, 15.1% of TRR in kidney and 20.2% of TRR in muscle; and MS4, 10.9% of TRR in milk (see Figures 2 and 4 for structures).

Conclusion 3: The portion of the total radioactive residue characterized and/or identified ranged from 26.3% in liver to 53.9% in fat. Unidentified metabolites each represented less than 10% TRR or less than 0.05 ppm, in all tissues except liver.

It appears that storage stability data were not provided for the aqueous fractions analyzed in Supplement 1 to the metabolism report. The main report indicates that extracted samples were counted during October 1991; Supplement 1 indicates that additional sample analysis was performed during July 1992. Samples therefore could have been stored frozen for 9 months or more before analysis.

Conclusion 4: Registrant should provide frozen storage data for the samples analyzed in Supplement 1 to Report R23979/FK1206. If samples were stored for more than 6 months, registrant should provide storage stability data. Ideally, data should indicate that the identity of residues did not change during the period between collection and final analysis. If data are not available to indicate chromatographic profiles of extracted samples shortly after collection, then data indicating that total radioactivity in the fractions of interest did not change significantly during storage would be acceptable.

The characterization and/or identification of residues analyzed is satisfactory. However, more than 20% of the TRR in liver was not analyzed (see Conclusion 1). The residues analyzed in liver ultimately were derived from the initial methanol and methanol:water extraction. Registrant reported that the methanol Soxhlet treatment was applied to liver, but did not report recovery from this treatment. The residues recovered by methanol Soxhlet treatment should be further analyzed, if they represent greater than 10% of TRR in liver.

Recommendation: The characterization and/or identification of residues analyzed is satisfactory, but further work is necessary to upgrade this metabolism study to an acceptable level. The residues in liver remaining after initial methanol and methanol:water extraction should be extracted by exhaustive methanol Soxhlet treatment. If residues greater than 10% of liver TRR are released by this treatment, they should be further extracted, if appropriate, and analyzed. The identity of any metabolite representing greater than 10% of TRR and greater than 0.05 ppm should be confirmed by a second method. Such analysis should be supported by appropriate storage stability data. If data are not available to indicate chromatographic profiles of



CBRS 10589, Imazalil, Metabolism in Goat, p. 17 of 16

extracted samples shortly after collection, then data indicating that total radioactivity in the fractions of interest did not change significantly during storage would be acceptable.

Analytical Method Submission

This review assignment also included two documents on analytical methods:

A Validated Gas Chromatographic Method for the Determination of Total Regulable Residues of Imazalil on Bananas, Janssen Report No. 56(AGR16), August 10, 1992 (MRID 42454803), and

A Gas-Liquid Chromatographic Method for Determining Total Regulable Residues of Imazalil in Citrus Fruit and Process Fractions, Janssen Report No. R23979/AGR18, August 14, 1992 (MRID 42454804).

It should be noted that an additional document on an analytical method for plant commodities, MRID 42454805, was assigned under DP Barcode 182707, CBRS No. 10602. In order to facilitate more efficient review, the analytical methods included with this assignment will be transferred to CBRS No. 10602, and will be reviewed as part of that assignment.

Conclusion 5: This assignment also included documents on analytical methods in plants (MRID 42454803 and 04). The assignment under DP Barcode No. D182707. CBRS No. 10602 consists of another analytical method in plants (MRID 42454805). For more efficient review, the analytical methods under this assignment will be transferred to CBRS No. 10602 and will be reviewed as part of that assignment.

Attachment: Unofficial Imazalil Residue Chemistry Summary cc (with Attachment): Abbotts, Imazalil List B File cc (without Attachment): Circ, RF, Imazalil SF RDI:FBSuhre:2/16/93:MSMetzger:2/16/93:EZager:2/16/93

H7509C:CBII-RS:JAbbotts:CM-2:Rm805A:305-6230:2/17/93

Through 2/17/93

